ehp

LESSON:

What Are Biomarkers?

Summary: Students develop reading, interpretation, summary, and vocabulary skills while learning about cutting-edge research in the use of biomarkers to understand the role of environmental exposures in disease.

Lesson Type: Focus Lesson—This lesson type develops students' skills and topical understanding by having them read and interpret information from an in-depth article.

***EHP* Article:** "Signs of the Times: Biomarkers in Perspective"
EHP Student Edition, March 2007, p. A701–A705
http://www.ehponline.org/docs/2006/114-12/focus-abs.html

Objectives: By the end of this lesson, students should be able to

1. write simple and accurate definitions in their own words for biology vocabulary using a dictionary and contextual information from an article; and
2. order and summarize an example from the article describing how biomarkers are being used to identify and describe a "continuum of biological events."

Class Time: 1.5–2 hours

Grade Level: 10–12

Subjects Addressed: Biology, Biochemistry, Health, Environmental Health

Prepping the Lesson (15 minutes)

INSTRUCTIONS:

1. Download the entire March 2007 *EHP Student Edition* at http://www.ehponline.org/science-ed/, or download just the article "Signs of the Times: Biomarkers in Perspective" at http://www.ehponline.org/docs/2006/114-12/focus-abs.html.
2. Review the Background Information, Instructions, and Student Instructions.
3. Decide how you would like the students to proceed with Step 1 of the lesson. Depending on available resources, students could use the Internet or an up-to-date medical or biological dictionary to help them define vocabulary words. Have students learn how to look up and sort through various definitions is an important skills builder. If you do not have access to those resources, a student handout titled "Definitions Resource Sheet" is provided for you to copy and distribute.
4. Make copies of the Student Instructions and the article.

MATERIALS (per student):

- 1 copy of the March 2007 *EHP Student Edition*, or 1 copy of "Signs of the Times: Biomarkers in Perspective," preferably in color
- 1 copy of the Student Instructions
- Internet access, medical dictionaries, and/or copies of the student handout titled "Definitions Resource Sheet"

VOCABULARY:

- adducts
- aflatoxin
- biologically effective dose
- biomarkers
- biomarkers of biologically effective dose
- continuum of biological events
- disease susceptibility
- effect biomarkers

- exposure biomarkers
- metabolically transformed
- molecular biology
- molecular epidemiology
- susceptibility
- susceptibility biomarkers

BACKGROUND INFORMATION:
The article provides sufficient background information for this lesson.

RESOURCES:
Environmental Health Perspectives, Environews by Topic page, http://ehp.niehs.nih.gov/. Choose Chemical Exposures, Standards

Biology-Online Editable Wiki Dictionary, http://www.biology-online.org/dictionary

Dictonary.com, http://www.dictionary.com/ or http://www.dictionary.reference.com/ (same website)

International Labour Organisation Encyclopaedia of Occupational Health and Safety, "Biomarkers," http://www.ilo.org/encyclopaedia/?doc&nd=857400331&nh=0

Implementing the Lesson

INSTRUCTIONS:

1. Distribute the Student Instructions, the article, and, if needed, the "Definitions Resource Sheet."
2. Refer to the Student Instructions and read Step 1 aloud to the class, or have a student read the instructions aloud.
3. Instruct the students on how you would like them to complete Step 1. A suggested protocol is to have the students read the article and define the words individually and then work in groups of 3 or 4 to share, clarify, and refine their definitions. Each student should write their group's final definitions on a separate piece of paper and turn in the group draft with the draft of their individual definitions.

   Depending on your students' reading level and experience with defining words from an article, you may need to walk them through the first one or two vocabulary words to clarify what constitutes a good definition (clear, concise, accurate, uses simple language, and does not use a derivative of the vocabulary word within the definition). The Assessing the Lesson section should be helpful in this task.

   Inform students that the goal of defining these words is to develop their ability to find and distill information in a meaningful way. The article itself provides definitions of some of the vocabulary words, but those definitions may still be too complex for students to fully understand the meaning (you may want to remind students that they are reading articles from a journal that scientists read, thus the definitions often use more complex language). Ideally students will write a definition in their own words, combining information from different places in the article and from other resources like Dictionary.com, a medical or biological dictionary, or a copy of the "Definitions Resource Sheet."
4. After the students have completed Step 1, instruct them to complete Step 2 individually. Be prepared to help students identify and distill the important information in the article about how biomarkers known as DNA–aflatoxin adducts have helped identify or describe the **continuum of biological events** toward the development of liver cancer. Students who need more support could be guided by asking them the questions below:
   - Describe how or why the DNA–aflatoxin adduct is a useful **exposure biomarker**.
   - Describe how or why the DNA–aflatoxin adduct is a useful **effect biomarker**.
   - Describe what was discovered that may make DNA–aflatoxin adducts useful as a **susceptibility biomarker**.

NOTES & HELPFUL HINTS:

1. Biochemistry or advanced biology classes could extend this lesson by having the students investigate a specific biomarker discussed in the article.
2. The article "Signs of the Times: Biomarkers in Perspective" describes the history of the development of biomarkers. Students could identify, describe, and analyze the scientific method in action for biomarkers.
3. Collaborate with a language arts teacher when doing this activity.

Aligning with Standards

SKILLS USED OR DEVELOPED:

- Classification
- Communication (note-taking, oral, written—including summarization)
- Comprehension (listening, reading)
- Critical thinking and response
- Technological design

SPECIFIC CONTENT ADDRESSED:

- Biomarkers
- Molecular biology
- Disease development and progression
- History of science
- Biotechnology

NATIONAL SCIENCE EDUCATION STANDARDS MET:

Science Content Standards

Unifying Concepts and Processes Standard

- Systems, order, and organization
- Evidence, models, and explanation
- Change, constancy, and measurement

Science as Inquiry Standard

- Understanding about scientific inquiry

Life Science Standard

- The cell
- Molecular basis of heredity
- Matter, energy, and organization in living systems
- Behavior of organisms

Science and Technology Standard

- Abilities of technical design
- Understanding about science and technology

Science in Personal and Social Perspectives Standard

- Personal and community health
- Environmental quality
- Natural and human-induced hazards
- Science and technology in local, national, and global challenges

History and Nature of Science Standard

- Science as a human endeavor
- Nature of scientific knowledge
- Historical perspectives

Assessing the Lesson

Step 1: Students should provide clear, concise definitions, preferably in their own words. If students are turning in both individual and group definitions, you can partially assess a student's contribution to the group (i.e., if the individual definitions are incomplete, their contribution to the group may have been limited), as well as the individual student's ability to define words placed within the context of an article.

Below are examples of good, acceptable, and unacceptable definitions. The unacceptable definitions may be a result of students copying word-for-word from the text, with the definition that is copied either being overly complex, using advanced terminology, or using part of the vocabulary word within the definition (e.g., "a biomarker is a marker for..."). A definition is also unacceptable if students are having difficulty discerning between the meaning of a word

and its uses, applications, or common associations. For example, a student may copy from the article the first real description they see for the word "biomarker" (i.e., biomarkers "reflect the individual's health status and risk at key time points") as the definition. But this is not a definition; it is a use or application of biomarkers. In contrast, a good definition that uses information from the *EHP Student Edition* article and the Dictionary.com website is "a specific physical trait or biologically produced chemical connected with a disease or health condition."

NOTE: Ideally a definition should be rewritten in the student's own words. However, sometimes a definition from a source is so clear, simple, and concise that it is difficult for students to write a new definition in their own words without compromising meaning. When a definition is copied from a source, students should place it in quotes and always cite the source.

biomarker

Good definition:

A specific physical trait or a measurable biologically produced change in the body connected with a disease or health condition.

Acceptable definitions that have been copied from the text:

From the *EHP Student Edition* article: "Biomarkers include physical parameters that can be clearly anchored to a disease or class of diseases."

From Dictionary.com: "A specific physical trait used to measure or indicate the effects or progress of a disease or condition."

Unacceptable as a stand-alone definition provided by the student (however, these may be used as examples within a definition; these are quotes from the *EHP Student Edition* article):

- "Biomarkers that reflect the individual's health status and risk at key time points."
- "Scientists rely on biomarkers to track each phase of the dose–response continuum, from exposure through effect."
- "In medicine, they can include measures such as heart rate or serum cholesterol, both of which correlate directly with cardiac disease risk. For environmental health purposes, biomarkers include a range of additional exposure-related indices, such as pollutant measures in tissues and bodily fluids; exposure-induced changes in cells, proteins, DNA, and other molecules; and inherited gene variations that influence how individuals respond to their environments. Single-nucleotide polymorphisms (SNPs), for instance, which are simple inherited gene variations, can increase or lessen disease susceptibility following environmental exposures."

biologically effective dose:

Good definition:

The amount of a chemical that causes important cell targets to turn on or respond.

Acceptable definition copied from the text:

"The amount of a chemical interacting with critical cellular targets."

exposure biomarkers:

Good definition:

A specific physical or chemical response used to measure or determine an exposure to a chemical or biological agent and how much of that agent entered the body.

Acceptable definition copied from the text (the weakness of using this definition includes using the words "marker" and "dose" as part of a definition that depends on existing background knowledge to fully understand):

"Markers of external exposure and of internal dose."

effect biomarkers:

Good definition:

A specific physical or chemical response used to measure or determine if a chemical or biological agent is harming health, is connected with a specific disease, or is connected with early biological events that harm health or lead to disease.

Acceptable definition copied from the text that uses more complex terminology, perhaps limiting the student's complete understanding:

"Markers of health impairment or recognized disease, early disease precursors, or peripheral events that predict health impairment."

susceptibility biomarkers:

Good definition:

Specific physical, chemical, genetic, or behavioral characteristics of a person that can make him or her more likely to get sick from a biological or chemical agent. These characteristics could increase the amount of a chemical or biological agent in the body or increase the ability of a chemical to cause damage to their body.

Acceptable definitions that use more complex terminology (students may need to look up the word "susceptibility" to help refine their definition):

From the *EHP Student Edition* article: "Intrinsic genetic or other characteristics or preexisting diseases that result in an increase in internal dose, biologically effective dose, or target tissue response."

From Dictionary.com ("susceptibility"): "The state of being predisposed to, sensitive to, or of lacking the ability to resist something (as a pathogen, familial disease, or a drug)."

continuum of biological events:

Good definition:

The series of changes in the body from the point of exposure to a chemical or biological agent to the resulting disease.

Acceptable definition copied from the text that uses more complex terminology:

"Biomarkers could be used to delineate each event within the continuum, from exposure, to internalized dose, to biologically effective dose, to altered molecular structure, and finally to clinical disease."

adduct (NOTE: use the biological definition rather than the physiological or chemical definitions):

Good definition:

A new molecule that is created when a chemical binds or interacts with a biological molecule such as protein or DNA.

Acceptable definition copied from Biology-Online.org:

"A complex that forms when a chemical binds to a biological molecule, such as DNA or a protein."

Unacceptable as a stand-alone definition, but parts could be used in a definition (copied from the *EHP Student Edition* article text):

"As biomarkers, adducts serve a number of key purposes: they reflect individual exposures, and they also focus exposures on key toxicological targets within the cell. What's more, adducts can provide evidence for metabolic steps in the exposure–response continuum. That's because some compounds can bind with proteins or DNA only after being metabolically transformed."

metabolite:

Good definition:

A new chemical or molecule created in the body by cellular biological processes.

Unacceptable as a stand-alone definition because it uses part of the vocabulary word as the definition:

From Dictionary.com: "A product of metabolic action."

Step 2: Using aflatoxin as an example, describe how DNA–aflatoxin adducts have helped identify or describe the **continuum of biological events** towards the development of liver cancer. Be sure to meaningfully and accurately incorporate as many of the vocabulary words from Step 1 as possible and summarize the information from the *EHP Student Edition* article in your own words.

Students' answers should be simple, clear, and concise, and should demonstrate understanding of the vocabulary words and information they read in the article. Some students may pick up on how the discovery of a good biomarker advanced the scientific understanding of a possible mechanism for liver cancer caused by aflatoxin (a mutation in the *p53* tumor suppressor gene).

Students who need more support or guidance could be asked to answer the following questions:

- Describe how or why the DNA–aflatoxin adduct is a useful exposure biomarker.
- Describe how or why the DNA–aflatoxin adduct is a useful effect biomarker.
- Describe what was discovered that may make DNA–aflatoxin adducts useful as a susceptibility biomarker.

A sample answer is provided below.

An aflatoxin-specific DNA adduct was found in the urine of people who were exposed to the toxic mold product aflatoxin. This DNA adduct was determined to be a useful exposure biomarker because it positively corresponded with a person's aflatoxin dose (i.e., the amount of the biomarker found in the person's urine increased as the dose or exposure to aflatoxin increased.) The DNA–aflatoxin adduct was also found to be a useful effect biomarker because it was shown to be strongly associated with the disease outcome of liver cancer. Various DNA–aflatoxin adducts may also be useful as susceptibility biomarkers because there are differences in the amounts and types of adducts produced in people who have liver cancer and/or the hepatitis B virus. The discovery of the DNA–aflatoxin adduct led to the identification of a potential specific mechanism for liver cancer, which is a mutation in the *p53* tumor suppressor gene.

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Give us your feedback! Send comments about this lesson to ehpscienceed@niehs.nih.gov.

Student Instructions: What Are Biomarkers?

Step 1: You are going to learn about the intersection of biology, health, and the environment at the molecular level. An exciting new cutting-edge field of science is looking at specific changes in the body, called biomarkers, to identify a person's exposure to a biological or chemical agent in the environment and the body's response to that exposure over time.

Read the article "Signs of the Times: Biomarkers in Perspective." As you read through the article, define the eight vocabulary words or phrases below that are used in the article (the words are listed in the order they appear in the article). Some of these words are well defined in the article. For others, you will need to combine information from the article with definitions from other sources. If the meaning is still unclear after writing the definition of a word, you should keeping looking up definitions from different sources until you understand the meaning of the word. Try to write definitions in your own words since this helps you process and remember the information. Each definition should be simple yet detailed enough that someone who knows nothing about the topic could read it and understand the meaning.

a. biomarker:

b. biologically effective dose:

c. exposure biomarkers:

d. effect biomarkers:

e. susceptibility biomarkers:

f. continuum of biological events:

g. adduct:

h. metabolite:

Step 2: Using aflatoxin as an example, describe how DNA–aflatoxin adducts have helped identify or describe the **continuum of biological events** toward the development of liver cancer. Be sure to meaningfully and accurately incorporate as many of the vocabulary words from Step 1 as possible and summarize the information from the *EHP Student Edition* article in your own words.

Definitions Resource Sheet

These definitions may be used with the information in the article to help you write your own simple and accurate definitions of the vocabulary words or phrases listed in Step 1 on the Student Instructions.

adduct (from Biology-Online.org): "A complex that forms when a chemical binds to a biological molecule, such as DNA or a protein."

biomarker (from Dictionary.com): "A specific physical trait used to measure or indicate the effects or progress of a disease or condition."

metabolite (from Dictionary.com): "A product of metabolic action."

metabolism (from Dictionary.com): "The sum of the physical and chemical processes in an organism by which its material substance is produced, maintained, and destroyed, and by which energy is made available."

susceptibility (from Dictionary.com): "The state of being predisposed to, sensitive to, or of lacking the ability to resist something (as a pathogen, familial disease, or a drug)."